



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference SCB 761 PCT		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)	
International application No. PCT/EP 03/04100	International filing date (day/month/year) 18.04.2003	Priority date (day/month/year) 23.04.2002	
International Patent Classification (IPC) or both national classification and IPC C07C49/733			
Applicant INDENA S.P.A. et al			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand 12.11.2003		Date of completion of this report 04.02.2004	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Jardon Alvarez, J Telephone No. +49 89 2399-8325 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/04100**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-13 as originally filed

Claims, Numbers

1-9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b));
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
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International application No. **PCT/EP 03/04100**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-9
	No: Claims	
Inventive step (IS)	Yes: Claims	1-9
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-9
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

D1: WO - A - 99 64388 A

D2: WO - A - 99 41220 A

1. The subject-matter of the claims fulfils the requirements of Article 33(2) - (4) PCT.
 - 1.1. None of the cited documents discloses hyperforin and adhyperforin derivatives of formula (I) as given in claim 1 for use as medicaments (claims 1 to 7), the compounds of claim 8 or the compositions of claim 9. The subject-matter of the claims is then novel (art. 33(2) PCT).
 - 1.2. Hyperforin and adhyperforin derivatives such as salts or hydroxyfunctionalized derivatives and its use for prophylaxis and treatment of neurodegenerative diseases such as Alzheimer is already known (see D2, claims and abstract and D1, claims). These known compounds are said to show some drawbacks such as low stability (see page 2 of the present description).

The problem to be solved by the present application can then be seen as to provide further related compounds useful also in the treatment of neurodegenerative activity and having a high stability. This problem is solved by the use of the compounds of the formula (I) as given in claim 1 having all double bonds of the isoprene chains hydrogenated and/or the keto groups at the 1 - 10 positions reduced to hydroxy. These compounds are said to have a high stability and surprisingly also possess higher activity than hyperforin and adhyperforin (see page 3 and experimental results on pages 8 and 9).

There is no hint to the advantageous properties of said compounds in the available documents which deal with different derivatives of hyperforin and adhyperforin and therefore an inventive step is acknowledged for the subject-matter of claims 1 to 9 (Art. 33(3) PCT).